

TABLE 8

Compound of Example No.	Dose mg/kg	% of Rats With Lesions	Comments
vehicle		12.5	—
naproxen	25	75.0	—
7	100	87.5	no protection
10	100	37.5	protection
11	100	50.0	moderate protection

EXAMPLE 41

The assay of this Example measures the ability of the compounds tested to inhibit 5-lipoxygenase in human whole blood.

This assay is carried out as follows:

Blood is obtained in 50–100 ml quantities from male donors. White blood cell counts and differentials are made. Two ml of blood are placed in a 15 ml polypropylene test tube. Compounds are solubilized in dimethylsulfoxide and diluted 1:10 in 10% bovine serum albumin in phosphate buffered saline, pH 7.4 resulting in a final dimethylsulfoxide concentration of 0.1% in the blood. Then, compounds are added to the blood in a shaking water bath at 37° C. for 10 minutes prior to the addition of 30 μ M calcium ionophore (A23187; Sigma). After ionophore administration, whole blood samples are mixed and incubated for 20 minutes at 37° C. in a shaking water bath. Incubation is terminated by placing samples in an ice bath and immediately adding ethylene glycol-bis-(β -aminoethyl ether)-N,N,N', N'-tetraacetic acid (10 mM). Samples are mixed and centrifuged at 1200=g for 15 minutes at 4° C. Preparation of samples for evaluation by RIA or ELISA is carried out by the following protocol. Plasma is removed from sample tubes, placed in 15 ml polypropylene test tubes containing 8 ml methanol, and then vortexed to precipitate protein. Samples are stored at -70° C. overnight. The next day, samples are centrifuged at 200 \times g for 15 minutes at 4° C. to pellet the precipitate. Samples are dried in a Savant speed vac concentrator, reconstituted to original volume with ice cold RIA or ELISA buffer, and stored at -70° C. until assayed. The assay for eicosanoids (LTB₄, TxB₂, and PGE₂) is performed as described by the manufacturer of the [³H]-RIA kit or ELISA kit (LTB₄-Amersham, TxB₂ and PGE₂-Caymen Chemical).

The total eicosanoid level in 2 ml of blood is calculated and reported as ng/10⁶ neutrophils. Significance is determined by a one-way analysis of variance with least significant difference (LSD) comparisons to control ($p \leq 0.05$) and IC₅₀'s (μ M) are determined by regression analysis (Finney, 1978). Drug effects are expressed as percent change from control values.

Compounds tested in vitro are solubilized in dimethylsulfoxide and diluted 1:10 in 10% bovine serum albumin in phosphate buffer saline resulting in a final dimethylsulfoxide concentration of 0.1% in the blood.

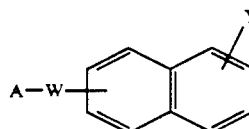
The results for compounds of the invention tested in this assay are presented in Table 9.

TABLE 9

Compound of Example No.	Dose (μ M)	% Inhibition of LTB ₄
A-64077	5	72
L-663,536	3	96
17	25	19
23	5	45
24	5	44
25	25	45
26	100	8
29	50	24
30	50	13

What is claimed is:

1. A compound having the formula



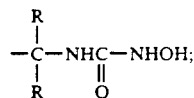
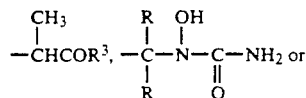
wherein

A is quinolinyl;

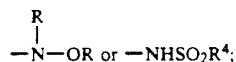
W is $-\text{CR}_2\text{O}-$, $-\text{CH}=\text{CH}-$ or $-\text{CH}=\text{CHC}-\text{H}_2\text{O}-$;

R is hydrogen or lower alkyl;

Y is



R³ is



R⁴ is phenyl or loweralkyl substituted phenyl; and the pharmaceutically acceptable salts thereof.

2. The compound of claim 1, having the name N-hydroxy- α -N-dimethyl-6-(2-quinolinylmethoxy)-2-naphthaleneacetamide dihydrate.

3. The compound of claim 1, having the name (S)-N-hydroxy- α -N-dimethyl-6-(2-quinolinylmethoxy)-2-naphthaleneacetamide.

4. The compound of claim 1, having the name α -methyl-N-[(4-methylphenyl)sulfonyl]-6-(2-quinolinylmethoxy)-2-naphthaleneacetamide.

5. The compound of claim 1, having the name N-methoxy- α -methyl-6-(2-quinolinylmethoxy)-2-naphthaleneacetamide.

6. The compound of claim 1, having the name (-)-N-[1-[6-(2-quinolinylmethoxy)-2-naphthalenyl]ethyl]-N-hydroxyurea.

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